UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/529,759	04/18/00	VIVIER E	A33131-PCT-U

021003
BAKER & BOTTS
30 ROCKEFELLER PLAZA
NEW YORK NY 10112

HM22/1026

EXAMINER	
CHAKRABARTI,A	
ART UNIT	**PAPER NUMBER**
1655	8

DATE MAILED: 10/26/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/529,759	Vivier et al.
Examiner	**Art Unit**
Arun Chakrabarti	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- *Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.*
- *If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.*
- *If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.*
- *Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).*
- *Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).*

Status

1) ☒ *Responsive to communication(s) filed on 8/30/01 and 10/11/01 .*

2a) ☒ *This action is* **FINAL.** 2b) ☐ *This action is non-final.*

3) ☐ *Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.*

Disposition of Claims

4) ☒ *Claim(s) 24-55 is/are pending in the application.*

4a) *Of the above, claim(s) _____ is/are withdrawn from consideration.*

5) ☐ *Claim(s) _____ is/are allowed.*

6) ☒ *Claim(s) 24-55 is/are rejected.*

7) ☐ *Claim(s) _____ is/are objected to.*

8) ☐ *Claims _____ are subject to restriction and/or election requirement.*

Application Papers

9) ☐ *The specification is objected to by the Examiner.*

10) ☐ *The drawing(s) filed on _____ is/are objected to by the Examiner.*

11) ☐ *The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.*

12) ☐ *The oath or declaration is objected to by the Examiner.*

Priority under 35 U.S.C. § 119

13) ☐ *Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).*

a) ☐ *All* b) ☐ *Some** c) ☐ *None of:*

1. ☐ *Certified copies of the priority documents have been received.*
2. ☐ *Certified copies of the priority documents have been received in Application No. _____ .*
3. ☐ *Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).*

**See the attached detailed Office action for a list of the certified copies not received.*

14) ☐ *Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).*

Attachment(s)

15) ☒ *Notice of References Cited (PTO-892)*

16) ☐ *Notice of Draftsperson's Patent Drawing Review (PTO-948)*

17) ☐ *Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____*

18) ☐ *Interview Summary (PTO-413) Paper No(s). _____*

19) ☐ *Notice of Informal Patent Application (PTO-152)*

20) ☐ *Other: .*

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of in Paper No. 7 is acknowledged. The traversal is on the ground(s) that there is no burden in examining the claims of Groups I and II together. This is not found persuasive because as the restriction makes clear, additional search of Group II would require review not only of the patents in Group I, but also the patents for Group II. Review of these additional searches is prima facie evidence of burden which is not rebutted.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 24-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Regarding claims 24, 25, and 40 the phrase "capable of" renders the claims indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. The metes and bounds of the claims are vague and indefinite.

Claims 32, 53 and 55 are indefinite and vague because the claims are written in the passive tense, "may be formed" (Claim 32) and "can be used" (Claims 53 and 55). Method claims should recite positive, active process steps, see Ex parte Erlich 3 USPQ 2d 1011 (BPA1 1986). This rejection may be overcome by amending the claims to recite the active tense, e.g., "forming", and "using".

Regarding claims 32, 53 and 55, the phrases "may be formed" (Claim 32) and "can be used" (Claims 53 and 55) render the claims indefinite because it is unclear whether the limitations following the phrases are part of the claimed invention.

Regarding claim 54, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 24-26, 28 and 32-39 are rejected under 35 U.S.C. 102 (b) as being anticipated by Bottino et al. (European Journal of Immunology, (1996), Vol. 26, pages 1816-1824)

Bottino et al. teach in vitro method of identifying the repertoire of NKR inhibitory or activatory immunoreceptors within a subject wherein the immunoreceptor is selected from the p58.2 target receptors (Abstract and Introduction, Page 1816 and Figures 1, 2 and 3), characterized in that it comprises:

a) at least one pair of oligonucleotides, one being designated 3' oligonucleotide and the other 5' oligonucleotide, the 3' and 5' oligonucleotides of the same pair being both capable, under hybridization conditions corresponding to incubation, of hybridizing to the DNA or to the cDNA of a target NKR receptor, or NKR counterpart, but not hybridizing, under the same hybridization condition with the DNA or the cDNA of an NKR receptor counterpart, or respectively of an NKR receptor, functional counterpart of the target receptor (Abstract and Introduction, Page 1816 and MATERIALS AND METHODS Section, Identification of PAX molecule-associated transcript Subsection, Page 1820, Column 2 to Page 1822, column 1 and Figure 8). The property of being capable of hybridization to a DNA or cDNA for 1 min in a buffer [20 mM Tris-HCl, pH 8.4; 50 mM Kcl; 2.5 mM MgCl2] at a temperature of between 50 degree centigrade and 65 degree centigrade approximately, is inherently present in the primer pairs disclosed by Bottino et al.

b) detecting hybridization between the nucleic acid encoding the NKR inhibitory or activatory immunoreceptor and the 3' or 5' oligonucleotide pairs (MATERIALS AND METHODS Section, Identification of PAX molecule-associated transcript Subsection, Page 1820, Column 2 to Page 1822, column 1 and Figure 8).

Bottino et al. teach a method, wherein the oligonucleotides are coupled to a radioactive marker (MATERIALS AND METHODS Section, Subsection 2.7).

Bottino et al. teach in vitro method, wherein hybridization between the nucleic acid sample and the 3' and 5' oligonucleotide pair is detected by PCR amplification (MATERIALS AND METHODS Section, Subsection 2.7).

Bottino et al. teach in vitro method, wherein the hybridization which may be formed comprises, in addition, the resolution, on a polyacrylamide gel, of the reaction mixture derived from the bringing into contact, as well as the visualization of the presence or of the absence of electrophoretic bands comprising the hybrids which may be formed (Figure 9).

Bottino et al. teach in vitro method, wherein the method is used to document the genotypic and expression repertoire of inhibitory and activatory immunoreceptors (Abstract and Figures 2, 3, 8 and 9).

Bottino et al. teach in vitro method, wherein the nucleic acid sample is derived from animal NK cells (Abstract and MATERIALS AND METHODS Section).

Bottino et al. teach in vitro method, wherein the nucleic acid sample is a cDNA library (MATERIALS AND METHODS Section, Subsection 2.5).

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. Claims 24-25, 29-30 and 32-39 are rejected under 35 U.S.C. 102 (a) as being anticipated by Hiby et al. (Molecular Immunology, (1997), Vol. 34, No. 5, pages 419-430).

Hiby et al. teach in vitro method of identifying the repertoire of NKR inhibitory or activatory immunoreceptors within a subject wherein the immunoreceptor is selected from the KIR p58.2 and 58.1 and the KAR p50.2 and 50.1 target receptors (Abstract and Table 2) characterized in that it comprises:

a) at least one pair of oligonucleotides, one being designated 3' oligonucleotide and the other 5' oligonucleotide, the 3' and 5' oligonucleotides of the same pair being both capable, under hybridization conditions corresponding to incubation, of hybridizing to the DNA or to the cDNA of a target NKR receptor, or target NKR counterpart, but not hybridizing, under the same hybridization condition with the DNA or the cDNA of an NKR receptor counterpart, or respectively of an NKR receptor, functional counterpart of the target receptor (Abstract and Table 3 and Page 425, column 1, second and third paragraph). The property of being capable of hybridization to a DNA or cDNA for 1 min in a buffer [20 mM Tris-HCl, pH 8.4; 50 mM Kcl; 2.5 mM MgCl2] at a temperature of between 50 degree centigrade and 65 degree centigrade approximately, is inherently present in the primer pairs disclosed by Bottino et al.

b)detecting hybridization between the nucleic acid encoding the NKR inhibitory or activatory immunoreceptor and the 3' or 5' oligonucleotide pairs (Abstract and Table 3 and Page 423, column 2, last paragraph to page 425, third paragraph and Figure 2).

Hiby et al. teach an in vitro method, wherein hybridization between the nucleic acid sample and the 3' and 5' oligonucleotide pair is detected by PCR amplification (Page 425, column 1, third paragraph and Figure 3).

Hiby et al. teach an in vitro method, wherein the method is used to document the genotypic and expression repertoire of inhibitory and activatory immunoreceptors (Abstract and Tables 2 and 3).

Hiby et al. teach in vitro method, wherein the nucleic acid sample is derived from human NK cells (Abstract and MATERIALS AND METHODS Section).

Hiby et al. teach in vitro method, wherein the nucleic acid sample is a cDNA library (MATERIALS AND METHODS Section, amplification of cDNAs subsection).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 24-28 and 32-39 are rejected under 35 U.S.C. 103(a) over Bottino et al. (European Journal of Immunology, (1996), Vol. 26, pages 1816-1824) in view of Matthews et al. (Analytical Biochemistry, (1988), Vol. 169, pages 1-25).

Bottino et al teach the method of claims 24-26, 28 and 32-39 as described above.

Bottino et al do not teach the method, wherein the marker is a fluorescence marker.

Matthews et al. teach the method, wherein the marker is a fluorescence marker (Table 3).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine a fluorescence marker of Matthews et al. in the in vitro method of identifying the repertoire of NKR inhibitory or activatory immunoreceptors of Bottino et al. since Matthews et al. state, "Most attention has focused on alternatives to radioisotopic labels because of the associated problems of safety, stability, and waste disposal (Page 5, Column 2, Labels Section, lines 3-7)". By employing scientific reason, an ordinary practitioner would have been motivated to substitute and combine a fluorescence marker of Matthews et al. in the in vitro method of identifying the repertoire of NKR inhibitory or activatory immunoreceptors of Bottino et al. in order to achieve the express advantages noted

by Matthews et al. of markers which has focused on alternatives to radioisotopic labels because of the associated problems of safety, stability, and waste disposal.

10. Claims 24-26, and 28-39 are rejected under 35 U.S.C. 103(a) over Bottino et al. (European Journal of Immunology, (1996), Vol. 26, pages 1816-1824) in view of Bandman et al. (U.S. Patent 6,307,021 B1) (October 23, 2001).

Bottino et al teach the method of claims 24-26, 28 and 32-39 as described above.

Bottino et al do not teach the method, wherein amplification is by nested PCR using a DNA polymerase.

Bandman et al. teach the method, wherein amplification is by nested PCR using a DNA polymerase. (Column 10, lines 45-51).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine amplification by nested PCR of Bandman et al. in the in vitro method of identifying the repertoire of NKR inhibitory or activatory immunoreceptors of Bottino et al. since Bandman et al. state, "Additionally, one may use PCR, nested primers, and PROMOTER FINDER libraries to walk in genomic DNA. This process avoids the need to screen libraries and is useful in finding intron/exon junctions (Column 10, lines 47-51)". By employing scientific reason, an ordinary practitioner would have been motivated to substitute and combine amplification by nested PCR of Bandman et al. in the in vitro method of identifying the repertoire of NKR inhibitory or activatory immunoreceptors of

Bottino et al. in order to achieve the express advantages, as noted by Bandman et al., of a process that avoids the need to screen libraries and is useful in finding intron/exon junctions.

11. Claims 24-26, 28, 32-39, and 50-55 are rejected under 35 U.S.C. 103(a) over Bottino et al. (European Journal of Immunology, (1996), Vol. 26, pages 1816-1824) in view of Finkel et al. (U.S. Patent 5,976,819) (November 2, 1999).

Bottino et al teach the method of claims 24-26, 28 and 32-39 as described above.

Bottino et al do not teach the method, wherein the method is used to predict or to monitor the acceptance or rejection by a subject of tissue or the safety of pathogenicity or the state of activation of T cells within a subject or the state of resistance of a subject to infection or screen for compositions which can be used to reduce the symptoms associated with proliferation disorders.

Finkel et al. teach the method, wherein the method is used to predict or to monitor the acceptance or rejection by a subject of tissue or the safety of pathogenicity or the state of activation of T cells within a subject or the state of resistance of a subject to infection or screen for compositions which can be used to reduce the symptoms associated with proliferation disorders (Column 1, lines 41-49).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the method used to predict or to monitor the acceptance or rejection by a subject of tissue or the safety of pathogenicity or the state of activation of T cells within a subject or the state of resistance of a subject to infection or

screen for compositions which can be used to reduce the symptoms associated with proliferation disorders of Finkel et al. in the in vitro method of identifying the repertoire of NKR inhibitory or activatory immunoreceptors of Bottino et al. since Finkel et al. state, "To develop compounds that regulate the activity of molecules involved in T cell function, there must be an understanding of the molecules and interactions involved in such T cell related disease (Column 1, lines 45-49)". By employing scientific reason, an ordinary practitioner would have been motivated to substitute and combine the method used to predict or to monitor the acceptance or rejection by a subject of tissue or the safety of pathogenicity or the state of activation of T cells within a subject or the state of resistance of a subject to infection or screen for compositions which can be used to reduce the symptoms associated with proliferation disorders of Finkel et al. in the in vitro method of identifying the repertoire of NKR inhibitory or activatory immunoreceptors of Bottino et al. in order to achieve the express advantages, as noted by Finkel et al., of a strategy to develop compounds that regulate the activity of molecules involved in T cell function, and an understanding of the molecules and interactions involved in such T cell related disease.

Allowable Subject Matter

12. No prior art rejections are made against claims 40-49.

Response to Amendment

13. In view of the response to amendment, all previous 112 (second paragraph) rejections have been withdrawn. However, new 112 (second paragraph) rejections have been included. All 102(a) and 102(b) rejections are hereby being maintained. Three new 103(a) rejections have been included.

Response to Arguments

14. Applicant's arguments filed on August 30, 2001, have been fully considered but they are not persuasive.

Applicant argues that 102(b) rejection as being anticipated by Bottino et al. (European Journal of Immunology, (1996), Vol. 26, pages 1816-1824) is not proper and should be withdrawn. This argument is not persuasive. In response to applicant's argument that the Bottino et al. reference fails to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., pairs of oligonucleotide primers that may be used to selectively amplify the target NKR immunoreceptors) are not recited in the rejected claim(s) 24-26, 28 and 32-39 . Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that 102(a) rejection as being anticipated by Hiby et al. (Molecular Immunology, (1997), Vol. 34, No. 5, pages 419-430) is not proper and should be withdrawn.

This argument is not persuasive. Applicant argues that Hiby reference teaches sequencing of the amplified fragments to identify the receptor and does not teach identification by hybridization only. This argument is not persuasive because in presence of open "comprising" language of the claim, any additional step (in this case sequencing of the amplified fragments) may be included in the method. Applicant is also suggested that hybridization is also another method of sequencing a target DNA molecule.

In view of the response to arguments, all 102(a) and 102(b) rejections are hereby properly being maintained.

Conclusion

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from

the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Chakrabarti
Patent Examiner
Art Unit 1655

October 24, 2001

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600